

REMARKS

Claims 1-12 remain in this application.

Rejections under 35 USC 103

The presently claimed process actually is substantively different from the process of D1 at least in the following aspects.

1) D- or L-tartaric acid, (R,S)-amlodipine and DMSO form a DMSO-solvate precipitate in D1, i.e., DMSO is a part of the solvate precipitate (see D1, especially the Examples), while D- or L-tartaric acid and (R,S)-amlodipine form a tartrate salt precipitate (not a solvate) in 2-butanone in the present invention. i.e., 2-butanone is not a part of the salt precipitate. Thus, DMSO is not only a solvent but also a reagent in D1, while 2-butanone is only a solvent in the present invention. Therefore, DMSO in the solvate precipitate may have to be removed by using other solvent, such as refluxing methanol in D1, while a solvent-free tartrate salt precipitate could be directly obtained by filtration in the present invention.

2) In addition, D-tartaric acid is used to obtain (S)-(-)-amlodipine (see D1, Examples 1-4) and L-tartaric acid is used to obtain (R)-(+)-amlodipine (see D1, Examples 5-8) in D1. On the contrary, L-tartaric is used to obtain (S)-(-)-amlodipine and D-tartaric is used to obtain (R)-(+)-amlodipine in the present invention. Thus, the reaction employed in D1 is different from the reaction of the present invention.

3) D1 discloses that the e.e. values of the obtained (S)-(-)-amlodipine and (R)-(+)-amlodipine are 98.4% and 98.5%, respectively (see Examples 3 and 8). In the present invention, the e.e. values of the obtained (S)-(-)-amlodipine and (R)-(+)-amlodipine are 99.0% and 98.8%, respectively (see Examples 1 and 2). Hence, the presently claimed process could reach higher e.e. value in comparison with D1.

4) According to the material safety data sheets of DMSO and 2-butanone (see the attached documents), DMSO has a boiling point of 189°C and an explosion limits of 3.5-42% and 2-butanone has a boiling point of 79-80°C and an explosion limits of 1.8-10%, which means higher cost is needed to use and recover DMSO in view of safety and energy consumption in comparison with 2-butanone.

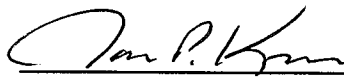
In view of the above discussion, D1 does not provide any teaching, suggestion or motivation to adopt the presently claimed process for producing enantiomers of amlodipine in industrial scale. D2 merely indicates that DMSO and 2-butanone are Class 3 solvents in view of their toxicity, but does not provide any information about using them in the separation of enantiomers of amlodipine. Hence, those skilled in the art would not obviously obtain the presently claimed process based on D1 and D2. Therefore, the pending claims 1-12 are non-obvious over D1 in view of D2 and Applicant respectfully requests allowance of those claims.

The Commissioner is hereby authorized to charge any additional fees which may be required with respect to this communication, or credit any overpayment, to Deposit Account No. 06-1135.

Respectfully submitted,

FITCH, EVEN, TABIN & FLANNERY

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